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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,707	09/30/2003	May Tom-Moy	10031347-1	8124

7590 04/23/2007

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EXAMINER	
LUM, LEON YUN BON	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/676,707	TOM-MOY ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-5, 7-8, 10-11, and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Science, 2002) (hereinafter "Park") as evidenced by Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000) (hereinafter "Fluke"), and in view of Guiseppi-Elie (US 5,312,762) and Eggers et al (US 5,891,630) (hereinafter "Eggers").

Park teaches the electrical detection of DNA by detecting binding between a capture oligonucleotide strand located in the gap between two fixed microelectrodes and a longer target oligonucleotide in solution (i.e. contacting feature with sample; probe disposed between first and second electrodes; polynucleotide). See page 1503, middle column, 2nd paragraph to right column, 1st paragraph. Park also teaches an array of 4 electrode pairs with a different oligonucleotide capture strand in the electrode gap (i.e. microarray with a plurality of features; plurality of targets are detected), wherein the oligonucleotide strands are immobilized onto a layer of SMPB-modified SiO_2 coated onto a Si wafer (i.e. pad of material disposed on the substrate; probe supported on pad of material). See page 1503, right column, 3rd paragraph to page 1504, left column, 2nd paragraph. In addition, Park teaches the step of increasing the sensitivity of the device by exposing the active component of the device to a solution of Ag(I) and hydroquinone (i.e. applying a source of metal ions). See page 1503, right column, 2nd paragraph. Park further teaches capacitance or conductivity measurements to determine the

number of target molecules that fill the gap (i.e. analyzing the results to detect the target). See page 1503, right column, 2nd paragraph. Furthermore, Park teaches measuring the resistance value across the gaps with a Fluke 189 multimeter (i.e. select one of the plurality of features to be interrogated; measuring the observable property at the selected feature). See page 1504, left column, 3rd paragraph to middle column, 1st paragraph. Since the Fluke 189 multimeter can only perform one measurement at a time, the detection of the 4-electrode pair array necessarily requires sequential detection, which indicates that the electrode pairs are selectively interrogated (i.e. repeating steps (c) and (d) to selectively interrogate each of the plurality of features). See Fluke Corporation, pages 2-4, 2-17, 3-6, and 3-7.

However, Park fails to teach that the pad of material is resistive, that the substrate comprises integrated addressing circuitry in operable relation to each of the plurality of features, and that fails to teach the step of providing a signal to the addressing circuitry to select one of the pluralities of features to be interrogated.

Guiseppi-Elie teaches chemoresistive biosensor devices with highly resistive membrane films between electrodes, in order to provide a biosensor with high detection sensitivity and low detection limit. See column 4, lines 12-68.

Eggers teaches detection circuitry 16 on-chip, wherein a varying signal of frequency can be applied to each site, in order to enable fast detection of hybridization for large DNA probe arrays. See column 4, lines 16-18; column 7, lines 30-32 and lines 44-46; and Figure 1.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Park with highly resistive membrane films between electrodes, as taught by Guiseppi-Elie, in order to provide a biosensor with high detection sensitivity and low detection limit. The benefit of having greater sensitivity provides the motivation to combine the teachings of Park and Guiseppi-Elie. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in including the resistive membrane film of Guiseppi-Elie in the method of Park, since Park teaches biosensors with electrodes, and the membrane of Guiseppi-Elie is capable of accommodating biological detection using electrodes.

It would also have been obvious to one of ordinary skill in the art at the time of the invention to modify the method and apparatus of Park with detection circuitry 16 on-chip, as taught by Eggers, in order to enable fast detection of hybridization for large DNA probe arrays. The detection circuitry of Eggers therefore provides an advantage over the multimeter of Park since the detection circuitry is able to interrogate a large number of electrode pairs in a short amount of time, whereas the handheld multimeter of Park et al would require a large amount of time to test each electrode pair in a large array. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the detection circuitry of Eggers, in the apparatus of Park, since Park teaches dual electrodes to detect hybridization in an array, and the detection circuitry of Eggers is connected to a plurality of electrode pairs that also detect hybridization.

Regarding claims 3-5, Park teaches that the target oligonucleotide is attached to Au nanoparticles at one end (i.e. gold nanoparticle label) and that Ag(I) and hydroquinone is added after the binding of target and capture oligonucleotides (i.e. attaching a label to target prior to applying the enhancement reaction; deposits metal). See page 1503, right column, 1st paragraph; and Figure 1 and caption.

Regarding claim 11, Eggers teaches circuitry for processing information related to target detection. See column 4, lines 31-33.

5. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Science, 2002) (hereinafter "Park") as evidenced by Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000) (hereinafter "Fluke"), and in view of Guiseppi-Elie (US 5,312,762) and Eggers et al (US 5,891,630) (hereinafter "Eggers") as applied to claims 1 and 3 above, and further in view of Cheung (US 5,132,242).

Park, Guiseppi-Elie, and Eggers references have been disclosed above, but they fail to teach that the label is attached to the target via a biotin-avidin conjugate binding pair.

Cheung teaches conjugation of DNA to microspheres using avidin and biotin, in order to take advantage of the strong non-covalent interaction between avidin and biotin. See column 10, lines 46-53.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Park, Guiseppi-Elie, and Eggers with conjugation of DNA to microspheres using avidin and biotin, as taught by Cheung, in order to take

advantage of the strong non-covalent interaction between avidin and biotin. The avidin-biotin conjugation to connect DNA to microspheres, as taught by Cheung, provides an advantage over the oligonucleotide-modified particles of Park, Guiseppi-Elie, and Eggers, since the avidin-biotin conjugation provides a strong interaction that would not allow dissociation of the microspheres from the bound targets and result in false negatives. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the avidin and biotin binding pairs, as taught by Cheung, in the method of Park, Guiseppi-Elie, and Eggers, since Park, Guiseppi-Elie, and Eggers et al teach particles bound to nucleic acids, and the avidin and biotin binding pairs of Cheung are able to conjugate microspheres, a type of particle, to nucleic acids.

6. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Science, 2002) (hereinafter "Park") as evidenced by Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000) (hereinafter "Fluke"), and in view of Guiseppi-Elie (US 5,312,762) and Eggers et al (US 5,891,630) (hereinafter "Eggers") as applied to claim 8, and further in view of Nayak (US 4,789,628).

Park, Guiseppi-Elie, and Eggers references have been disclosed above, but they fail to teach that the pad of resistive material comprises a plurality of segments with fissures between the segments.

Nayak teaches a plurality of spaced projections within a well with probes immobilized thereon, in order to increase the surface area for specific binding in assays

that may have a low concentration of substances. See column 3, line 51 to column 4, line 10; and column 6, line 62 to column 7, line 19.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Park, Guiseppi-Elie, and Eggers with a plurality of spaced projections within a well with probes immobilized thereon, as taught by Nayak, in order to increase the surface area for specific binding in assays that may have a low concentration of substances. By replacing the planar surface of Park et al and Eggers et al with the projections of Nayak, the apparatus of Park, Guiseppi-Elie, and Eggers would have the advantage of being able to detect specific binding with a sample solution having a low concentration of target. This advantage therefore provides the motivation to combine the projections of Nayak in the apparatus of Park, Guiseppi-Elie, and Eggers. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in including the projections of Nayak in the apparatus of Park, Guiseppi-Elie, and Eggers, since Park, Guiseppi-Elie, and Eggers teach probes immobilized on a surface for assay purposes, and the projections of Nayak are one example of a surface that can immobilize probes for an assay.

7. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Science, 2002) (hereinafter "Park") as evidenced by Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000) (hereinafter "Fluke"), and in view of Guiseppi-Elie (US 5,312,762) and Eggers et al (US 5,891,630) (hereinafter "Eggers")

as applied to claim 8, and further in view of Mallet et al (US 6,660,533 B2) (hereinafter "Mallet").

Park, Guiseppi-Elie, and Eggers references have been disclosed above, butthey fail to teach that the pad of resistive material is metal oxide.

Mallet teaches metal oxides surfaces, in order to provide an immobilization that is engenders very good signal to background noise ratios, and stable immobilization. See column 2, lines 45-53.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Park, Guiseppi-Elie, and Eggers with metal oxides surfaces, as taught by Mallet, in order to provide an immobilization that is engenders very good signal to background noise ratios, and stable immobilization. By providing good signal to background noise ratios, the binding of Park, Guiseppi-Elie, and Eggers would be more accurately detected. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the metal oxide surfaces of Mallet, in the apparatus of Park, Guiseppi-Elie, and Eggers, since Park, Guiseppi-Elie, and Eggers teach biomolecule immobilization onto surfaces, and the metal oxide of Mallet is one type of surface that can immobilize biomolecules.

8. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Science, 2002) (hereinafter "Park") as evidenced by Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000) (hereinafter "Fluke"), and in view of Guiseppi-Elie (US 5,312,762) and Eggers et al (US 5,891,630) (hereinafter "Eggers")

as applied to claim 8 as applied above, and further in view of Sandstrom (US 6,545,758 B1).

Park, Guiseppi-Elie, and Eggers references have been disclosed above, but they fail to teach at least one reference feature in operable relation to the addressing circuitry.

Sandstrom teaches control sites on a microarray, in order to compare experimental probe sites to a reference or purposefully mismatched site for eliminating signal from background signal and nonspecific hybridization. See column 4, line 61 to column 5, line 17.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Park, Guiseppi-Elie, and Eggers with control sites on a microarray, as taught by Sandstrom, in order to compare experimental probe sites to a reference or purposefully mismatched site for eliminating signal from background signal and nonspecific hybridization. The control sites of Sandstrom therefore provide the advantage of determining accurate detection in the binding sites of Park, Guiseppi-Elie, and Eggers. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including control sites, as taught by Sandstrom, in the apparatus of Park, Guiseppi-Elie, and Eggers, since Park, Guiseppi-Elie, and Eggers teach an array of binding sites, and the control sites of Sandstrom can also be placed in an array of binding sites.

Response to Arguments

9. Applicant's arguments, see pages 5-8 of the response, filed on January 24, 2007, with respect to the rejection(s) of claim(s) 1-15 under 35 U.S.C. 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Park et al (Science, 2002) (hereinafter "Park") as evidenced by Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000) (hereinafter "Fluke"), and in view of Guiseppi-Elie (US 5,312,762) and Eggers et al (US 5,891,630) (hereinafter "Eggers").

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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